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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,828	01/24/2002	Xianqiang Li	26757-707	4192

21971 7590 03/11/2004

WILSON SONSINI GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 943041050

EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,828	LI ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/6/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. Receipt is acknowledged of a Response to a Restriction Requirement, which was dated on November 20, 2003.

Priority Claims

2. No foreign or domestic priority is claimed. Therefore, the effective filing date of the claims is the filing date of the case i.e., January 24, 2002.

Status of the Claims

3. Claims 1-80 were pending.

4. Applicant's response to the Restriction and/or Election of Species requirements is acknowledged (Applicant elected ***without traverse*** Group I, claims 1-22) and Applicants cancelled without prejudice claims 23-80 (see 11/20/2003 Response) thus obviating the need for the Examiner to withdrawn claims 23-80 from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

5. Applicants' election of species ***without traverse*** is also acknowledged (see 11/20/2003 Response, pages 4-5).

6. The Examiner further notes that Applicants' "withdrawn" claims are being examined on the merits because those claims have not been withdrawn by the Examiner and thus are still pending i.e., it is the Examiner's job to withdraw claims under 37 CFR 1.142(b), not Applicants (e.g., see 11/20/2003 response wherein Applicants purportedly withdrew claims 5-7, 9-10, 12-13, 15-16 and 18-19).

7. Therefore, claims 1-22 are examined on the merits in this action.

Information Disclosure Statement

8. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

9. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98 (b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on the form PTO-892, they have not been considered.

10. The references listed on applicant's PTO-1449 form have been considered by the Examiner. A copy of the form is attached to this Office Action.

Specification

11. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-22 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a written description rejection.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit (CAFC) which held that a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)

(bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)] (the case is referred to herein as "*Lilly*"). Here, the instant claims define the components of the claimed library only by their functional properties (e.g., their ability to bind to a transcription factor). The CAFC held this sort of functional definition insufficient to adequately describe the claimed product.

The Examiner further notes that Applicants' claims are broader in scope than those that were held to be impermissible in *Lilly* because, unlike Lilly, Applicants' claims encompass an infinite number of sequences. Here, Applicants claim a library of nucleic acid constructs comprising a cis element sequence with one or more copies of a cis element to which a transcription factor is capable of binding, a promoter sequence 3' relative to the cis element and a reporter sequence 3' relative to the promoter that comprises a variable sequence (see claim 1). The scope of these claims include an infinite number of sequences because the specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form said sequences (i.e., no structural features limitations are set forth). Furthermore, the specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form said transcription factors, which are used as a point of reference to functionally define Applicants' claimed sequences (i.e., Applicants are using inadequately described transcription factors to inadequately describe the claimed sequences). In addition, Applicants' "capable of binding" claim language further exacerbates this problem because the conditions under which a cis sequence will bind to a transcription factor are not specified. Consequently, there is no teaching that would allow a person of skill in the art to determine *a priori* that Applicants were in

possession of the full scope of the claimed invention at the time of filing because there is no common structural attributes that can link together *all* of the claimed sequences and/or the transcription factors to which said claimed sequences bind (e.g., there is no structure/function correlation set forth).

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant (the genus encompasses an infinite number of sequences, see above), Applicants' listing of a handful of sequences (e.g., see Figure 2; see also page 18, lines 15-21) is insufficient to teach the entire genus. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus. Thus, applicant was not in possession of the claimed genus.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. **Claim 1** recites the limitation "the library of constructs" in lines 3-4 and the last two lines. There is insufficient antecedent basis for this limitation in the claim. Therefore, claim 1 and all dependent claims are rejected under 35 USC 112, second paragraph.

B. For **claim 1**, the phrase "a reporter sequence 3' relative to the promoter sequence that comprises a variable sequence that varies within the library" is vague and indefinite. For example, it is not clear whether the "variable" sequence refers to the "promoter" sequence or to the "reporter" sequence. Applicants are requested to clarify and/or correct. Therefore, claims 1 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

C. For **claim 1**, the phrase "wherein a same cis element sequence is employed with a given reporter sequence within the library of constructs" is vague and indefinite. For example, it is not clear how the "same" cis element sequence can be employed with a given reporter sequence because each reporter "varies within the library" (i.e., see claim 1, lines 7; see also 35 U.S.C. 112, second paragraph rejection, part "B" above) and thus no two reporters or corresponding cis element sequences could be the "same." Applicants are requested to clarify and/or correct. Therefore, claims 1 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-13 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Kauffman et al (US Patent No. 6,100,035) (Date of Patent is **August 8, 2000**) (see IDS).

For ***claim 1***, Kauffman et al (see entire document) disclose "methods identifying cis acting nucleic acid elements" (see Kauffman et al, title and abstract), which anticipates claim 1. For example, Kauffman et al disclose a cis element sequence comprising one or more copies of a cis element to which a transcription factor is capable of binding, the cis element sequence varying within the library of constructs (e.g., see column 2, lines 36-44, "The invention further provides a plurality of isolated nucleic acid molecules that each contain one or more cis acting nucleic acid elements ... A plurality of isolated nucleic acid binding factors is also provided [i.e., the cis acting elements are "capable" of binding to transcription factors]"; see also column 6, last two paragraphs, "A diverse population of isolated nucleic acid molecules can be of completely random composition ... [and] includes nucleic acid molecules potentially containing cis acting nucleic acid elements"; see also column 7, paragraph 2, "As used herein, the term "nucleic acid binding factor" is ... [a] transcription factor[s]"; see also column 24, paragraph 1; see also column 23, paragraphs 2-3). In addition, Kauffman et al disclose a promoter sequence 3' relative to the cis element sequence and a reporter sequence 3' relative to the promoter sequence (e.g., see column 5, first full paragraph, "A cis acting nucleic acid element can be localized within the nucleic acid sequence it regulates, or

upstream [i.e., 5'] or downstream [i.e., 3'] thereof"; see also column 4, last paragraph, "The types of cis acting nucleic acids [include] ... promoter elements, enhancer elements and response elements"; see also paragraph bridging columns 1-2). Finally, Kauffman et al disclose that a same cis element sequence is employed with a given reporter sequence within the library of constructs (e.g., see column 6, last two paragraphs, "A diverse population of isolated nucleic acid molecules can be of completely random composition or of partially or completely known composition [i.e., contain the same "partial" or "whole" sequence]"; see especially column 4, last paragraph, "Although individual cis acting nucleic acid elements can be involved in the regulation of many different nucleic acids, a particular combination of cis acting nucleic acid elements can be specific for one or only a limited number nucleic acids [i.e., each reporter gets only one cis sequence]").

For ***claims 2-3***, Kauffman et al disclose priming sequences 5' and 3' relative to the variable sequences (e.g., see column 7, paragraph 1, "If desired, some or all of the isolated nucleic acid molecules can include, or be flanked at one or both ends by, known sequences, such as sequences homologous to oligonucleotide primers for the polymerase chain reaction (PCR), sequences containing restriction sites or detectable sequences"; see also column 12, paragraph 3; see also column 15, paragraph 3).

For ***claims 4-7***, Kauffman et al disclose at least 10, 20, 50 and 1000 different cis elements (e.g., see column 6, lines 30-55; see especially lines 53-55, "Such a population of about 10^{13} 20 different nucleic acid molecules inherently includes all possible cis acting nucleic acid elements of up to about 20 nucleotides in length").

For ***claims 8-10***, Kauffman et al disclose a cis element sequence that comprises at least two copies of the cis element (e.g., see column 2, lines 36-44, "The invention further provides a plurality of isolated nucleic acid molecules that each contain one or more [i.e., two, three or four] cis acting nucleic acid elements"; see also column 14, paragraph 1).

For ***claims 11-13***, Kauffman et al discloses a cis element that is between 5 and 50 base pairs (e.g., see column 5, lines 13-15, "A cis acting nucleic acid element is generally from about 4 to about 100 nucleotides in length, and is more typically from about 6 to about 25 nucleotides in length").

For ***claim 20***, Kauffman et al disclose that a plurality of reporters can be used (e.g., see column 3, lines 46-53, "The methods are advantageous in providing a means for simultaneously identifying nucleic acid binding factors that modulate a genetic activity of a plurality of nucleic acids"; see also column 27, lines 61-63, "This procedure advantageously allows the simultaneous identification of a plurality of genes [i.e., reporters]").

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kauffman et al (US Patent No. 6,100,035) (Date of Patent is **August 8, 2000**) and Morris et al (US Patent No. 6,458,530)(Filing Date is **April 4, 1996**).

For ***claims 1-13 and 20***, Kauffman et al teaches all the limitations stated in the 35 U.S.C. 102(b) rejection above (incorporated in its entirety herein by reference), which anticipates claims 1-13 and 20 and, consequently, also renders obvious claims 1-13 and 20.

The prior art teaching of Kauffman et al differs from the claimed invention as follows:

For ***claims 14-19***, the prior art teachings of Kauffman et al differ from the claimed invention by not specifically reciting the size of the variable sequence in the reporter e.g., at least 14 bases in length (see claim 14).

For ***claims 21-22***, the prior art teachings of Kauffman et al do not explicitly recite an "open reading frame" although it is undoubtedly implied from the molecular cloning techniques used i.e., the reporter wouldn't be expressed without it (e.g., see column 23, line 48).

However, Morris et al teaches the following limitations that are deficient in Kauffman et al:

For ***claims 14-19***, Morris et al (see entire document) disclose specially selected nucleic acid tags that contain variable regions between 8 and 150 nucleotides in length for labeling molecular, cellular and viral libraries which would encompass the nucleic

acid constructs of Kauffman et al (e.g., see Morris et al, Summary of Invention; see also column 3, paragraphs 2-3; see also claim 7).

For ***claim 21***, Morris et al disclose the use of open reading frames (e.g., see column 11, paragraph 3; see also example 1, especially column 24, lines 14-51).

For ***claim 22***, both Morris et al and Kauffman et al do not explicitly state that a stop codon is 3' relative to the reporters disclosed therein, but the Examiner contends that stop codons are typically used in the art and the reporter sequence would not have the proper length if it did not contain such a stopping point. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best,* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

It would have been obvious to one skilled in the art at the time the invention was made to make and use the variable reporters as taught by Morris et al with the cis acting nucleic acid library as taught by Kauffman et al because Kauffman et al explicitly states that "[n]ucleic acid chips and automated detection procedures are particularly advantageous in high-throughput screening procedures for identifying cis acting nucleic acid elements" (e.g., see Kauffman et al, column 16, lines 53-54), which would encompass the automated nucleic acid chips disclosed by Morris et al i.e., the references represent analogous art (e.g., see Morris et al, figure 5 disclosing a nucleic acid chip).

Furthermore, one of ordinary skill in the art would have been motivated to use the variable reporters as taught by Morris et al because the variable reporters "provide a much more cost-effective approach to screening" i.e., parallel screening saves time and money (e.g., see Morris et al, column 11, lines 60-62). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because both Morris et al and Kauffman et al teach general methods that can use recombinant DNA optionally with PCR techniques i.e., the methods are compatible (e.g., see Kauffman et al, column 15, last paragraph; see also Morris, column 3, paragraph 2).

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
March 2, 2004

BENNETT CELSA
PRIMARY EXAMINER